## **Centers for Disease Control and Prevention Center for Preparedness and Response**



# **Evaluating and Supporting Patients**Presenting With Fatigue Following COVID-19

Clinician Outreach and Communication Activity (COCA) Call

Thursday, September 30, 2021

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- Planners have reviewed content to ensure there is no bias.
- The presentation will not include any discussion of the unlabeled use of a product or a product under investigational use, except part of the presentation will address the use of COVID-19 vaccine outside of approved age group, except parts of the presentation will discuss treatments for COVID and long COVID which are all under investigational use.
- CDC did not accept commercial support for this continuing education activity.

## **Objectives**

At the conclusion of today's session, the participant will be able to accomplish the following—

- 1. Determine which clinical assessments and tests are needed for an individual patient with fatigue.
- 2. Explain how post-exertional malaise impacts patient management.
- 3. Describe how to apply health equity considerations to clinical care, activity management, and reconditioning of long COVID patients.

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- Using the Zoom Webinar System
  - Click on the "Q&A" button
  - Type your question in the "Q&A" box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.
- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

## **Today's Presenters**

#### Maureen Miller, MD, MPH

Research, Surveillance, and Management Unit Natural History/Post-COVID Conditions Team Epidemiology Task Force COVID-19 Response Centers for Disease Control and Prevention

#### Benjamin Abramoff, MD, MS

Assistant Professor of Clinical Physical Medicine and Rehabilitation Department of Physical Medicine and Rehabilitation Penn Medicine

#### Joseph E. Herrera, DO

Professor and System Chair of Rehabilitative Medicine Department of Rehabilitation and Physical Medicine Mount Sinai Health System

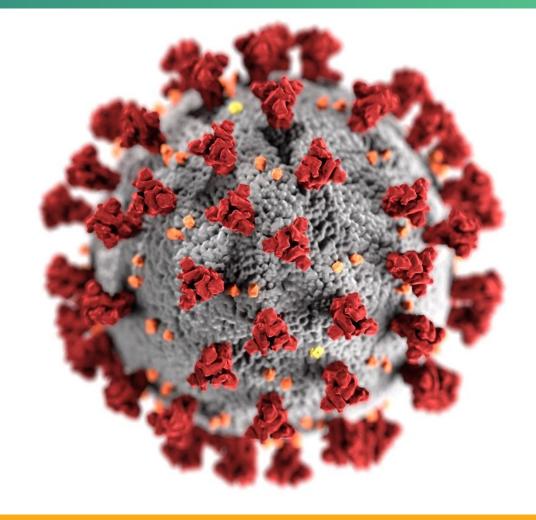
#### Monica Verduzco Gutierrez, MD

Professor and Chair of Physical Medicine and Rehabilitation Department of Physical Medicine and Rehabilitation UT Health San Antonio

# Evaluating and Supporting Patients Presenting With Fatigue Following COVID-19

CDC Clinician Outreach and Communication Activity (COCA)

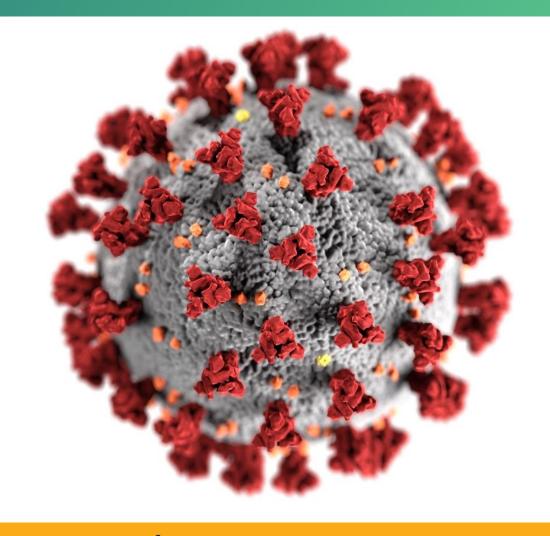
Maureen J. Miller, MD, MPH
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Natural History/Post-COVID Conditions Team





cdc.gov/coronavirus

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#### **Post-COVID Conditions**



- "Post-COVID conditions" is an umbrella term for the wide range of physical and mental health consequences that are present four or more weeks after SARS-CoV-2 infection, including by patients who had initial mild or asymptomatic acute infection
  - Associated with a spectrum of physical, social, and psychological consequences
  - Conditions are heterogeneous and attributable to different underlying pathophysiologic processes
- "Long COVID" is used by many patients for post-COVID conditions



# Proposed Framework Terminology for Conditions Following COVID-19

## General Consequences of Illness and Hospitalization

- Post ICU-syndrome
- Other complications of illness and treatment

### Post-Acute Consequences of SARS-CoV-2 Infection (PASC)

- System-specific pathology (e.g., lung fibrosis, stroke)
- Clinically significant symptoms with unclear pathology (e.g., ME/CFS\*-like, dysautonomia)
- Objective finding of unclear clinical significance (incidental)

These conditions frequently overlap, patients may experience any combination

# Wide Range of Longer-Term Adverse Health Outcomes from COVID-19

- Worsening pre-existing conditions and disabilities
  - People with disabilities may face barriers to adopting mitigation strategies and access to care
  - Prior workplace accommodations may not be sufficient
- Direct organ damage (lung, heart, kidney, nervous system damage from infection or hypercoagulability events)
- Debilitating symptoms with unclear pathology (fatigue, cognitive impairment, dysautonomia, post-exertional malaise, sleep problems, joint pain, tachycardia, etc.)
- Impaired mental health due to anxiety, depression, PTSD\*



# How Frequently Do Post-COVID Conditions Result in Disability?

- Systematic data on outcomes lasting longer than 12 months not yet available
- Most patients' symptoms slowly improve with time
  - Cohort study of COVID-19 participants found decrease in those reporting symptoms from 13.3% at ≥28 days to 2.3% at ≥12 weeks Nature 2021; 27: 626-31
  - Study from China on hospitalized COVID-19 patients found 88% returned to their original work by 12 months (this excluded 50% who were retired or not employed before COVID-19) <u>Lancet 2021; 398: 747-58</u>
- Extent of disability associated with persistent symptoms is unknown

Given size of pandemic, even 1% disability at one year will have impact



# **Evidence of Disability Associated with Post-COVID Conditions**

"Post-COVID-19 Symptoms Were Worse Than Cancer's Effect" — JAMA News summary of CDC's MMWR article JAMA 2021: 326; 692; MMWR 2021; 70: 967-971

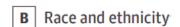
- Compared with patients referred for cancer rehabilitation, post-COVID patients had poorer physical health
  - More difficulty doing usual work (37.2% versus 20.4%) or participating in activities with friends (33.0% versus 18.8%)
  - Reduced endurance in 6-minute walk test (distance of 303m versus 377m)

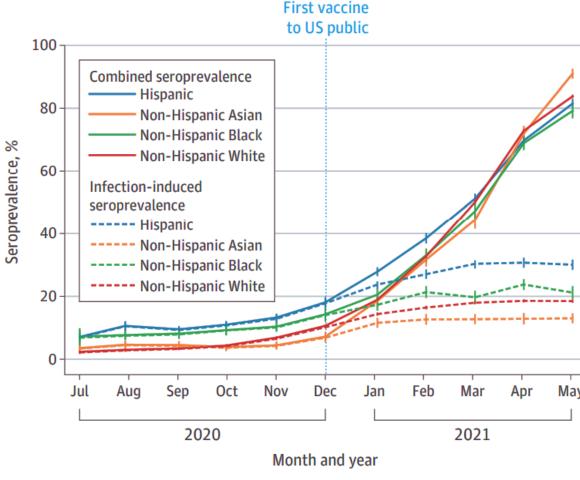
**Patient and advocacy groups'** reports have brought attention to disability associated with post-COVID conditions and the importance of including patients and caregivers in related research



## **Health Equity**

- Occurrence of post-COVID conditions is expected to reflect the disproportionate incidence of infection
- Infection-induced seroprevalence may suggest risk for developing long COVID by group
  - U.S. blood donor data indicate
    higher infection in Hispanic and
    Non-Hispanic Black persons than for
    other racial and ethnic groups





Jones JM et al. Estimated US Infection- and Vaccine-Induced SARS-CoV-2 Seroprevalence Based on Blood Donations, July 2021-May 2021. *JAMA* 3 Sept 2021.



## **CDC's Efforts Addressing Post-COVID Conditions**

- Examples of CDC's current efforts include:
  - Partnering with clinicians
  - Analyzing electronic health data
  - Establishing studies with external partners



#### **CDC Studies of Post-COVID Conditions**

- Enroll cohorts of patients with COVID-19 and controls without COVID-19
- Assess baseline health of the participants
- Monitor participants over time and for multiple years
- Assess outcomes of interest including:
  - Long-term immunologic response
  - Cardiovascular, respiratory, renal, neurological, psychiatric, mental and physical functioning
- Identify epidemiologic risk factors



## **CDC Will Continue to Explore:**

- Frequency, severity, and duration of post-COVID conditions
- Groups disproportionately impacted by post-COVID conditions
- Association of SARS-CoV-2 variants and vaccination with the incidence of post-COVID conditions
- Models of health care to assure equity and access

## **Summary: What are Post-COVID Conditions?**

- New, returning, or ongoing health problems 4 or more weeks after infection
- Not uncommon
- May occur among patients with COVID-19 regardless of acute illness severity
- In addition to respiratory symptoms, patients may present with fatigue, sleeping difficulties, depression, anxiety, palpitations, joint pain, and postexertional malaise; changes in renal function, nervous and circulatory systems also reported

#### Next...



Clinical Guidance



Multidisciplinary collaborative consensus guidance statement on the assessment and treatment of fatigue in postacute sequelae of SARS-CoV-2 infection (PASC) patients

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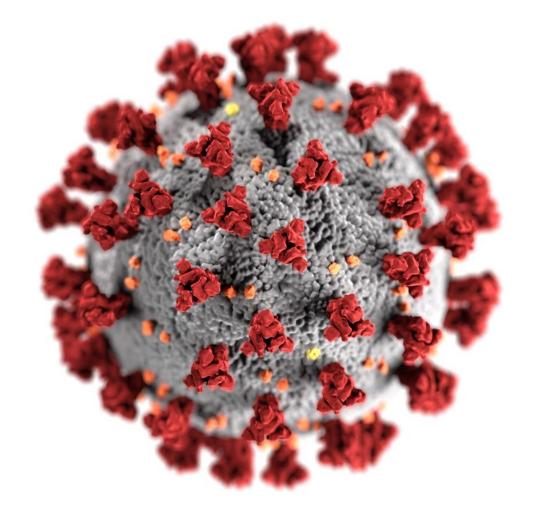
First published: 04 August 2021 | https://doi.org/10.1002/pmrj.12684



#### Thank you!

For more information, contact CDC 1-800-CDC-INFO (232-4636)

TTY: 1-888-232-6348 www.cdc.gov



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## Multi-Disciplinary Collaborative Consensus Guidance Statement on the Assessment and Treatment of Fatigue in Post-Acute Sequelae of SARS-CoV-2 infection (PASC) Patients

**September 30, 2021** 

**Faculty** 

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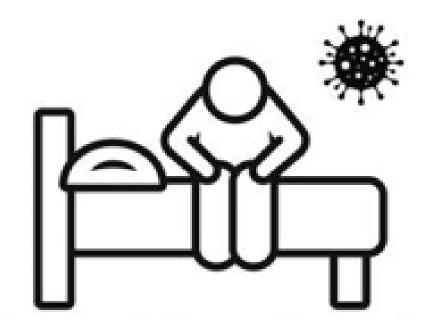


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## Millions of Americans have survived COVID-19



Months later, many still struggle to get out of bed.



## **Learning Objectives**

- Apply the PASC Consensus Guidance Statement Methods into everyday practice
- Identify and diagnose fatigue in individuals with PASC
- Utilize assessment recommendations
- Differentiate and apply appropriate PASC-related fatigue treatments
- Identify health equity considerations and examples in PASC-related fatigue
- Summarize the future directions in assessing and treating PASC-related fatigue

NOTE: These Consensus Guidance Statements are intended to reflect current best practices in patient assessment, testing, and treatments. They should not preclude clinical judgment and must be applied in the context of the specific patient, with adjustments for patient preferences, comorbidities, and other factors.



## **Consensus Statement Methodology**

**Collaborative Discussion of Areas of Prioritization** 

**Patient Perspectives** 

- Collaborative Symptom Discussion
- Establishment of Writing Group
- Writing Group: Considered collaborative discussion and literature to create draft recommendations
- Survey of writing group
- Parallel process for health equity considerations

Wave 1

Wave 2

- Candidate recommendations that emerged from writing group were sent to full PASC collaborative for vote.
- Statements with 80% consensus were retained.
- Statements with 60-80% approval were discussed further and refined, excluded or included in the discussion section but not as statement.

- Project team synthesis
   Collaborative input and returns
   recommendations to writing group
   for finalization
- Consensus vote
- Move to publication

Wave 3

Patient Perspectives

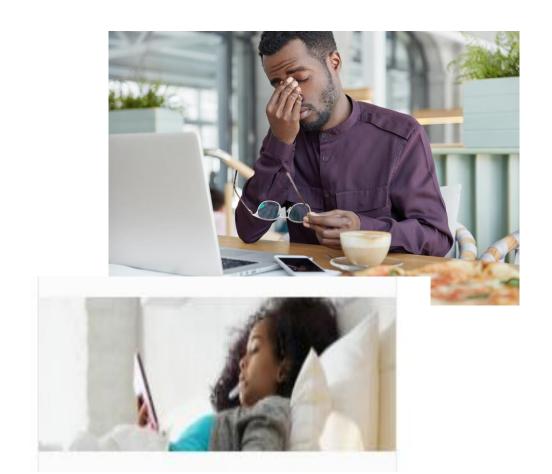
4-6 weeks from start to finish



## **Fatigue**

## aapm&r

- Fatigue is among the most common persistent symptoms following COVID-19 in both individuals who have been hospitalized and those who have not.
- Fatigue can be physical, cognitive, or emotional, mild to severe, intermittent to persistent, and affect a person's energy, motivation, and concentration
- Individuals are seeking care from their clinicians for fatigue following COVID-19



### **Fatigue Assessment Recommendations**



| #  | Statement   |
|----|---|
| 1  | Fatigue patterns throughout their normal day  |
| 1a | Patient responses to initiating and escalating activity on their fatigue.   |
| 1b | Changes in daily functioning and activity levels.   |
| 1c | Physical functioning and endurance should be assessed in order to inform activity and therapy recommendations.  |
| 2  | Assess for changes in activities of daily living, independent activities of daily living, school, work, and avocational (i.e., hobbies)   |
| 3  | A full patient history with review of pre-existing conditions should be conducted   |
| 4  | Patients should be evaluated for conditions that may exacerbate fatigue symptoms and warrant further testing and potential subspecialty referral (see Table 2)  |
| 5  | Investigate medications that may be contributing to fatigue. Of note, antihistamine, anticholinergic, and antidepressant/anxiolytic medications can contribute to fatigue in patients with PASC.  |
| 6  | Basic lab work-up should be considered in new patients or those without lab work-up in the 3 months prior to visit including complete blood count with differential, chemistries including renal and hepatic function tests, thyroid stimulating hormone, c-reactive protein or erythrocyte sedimentation rate, and creatinine kinase.  Other laboratory tests may be considered based on the results of the above tests or if there is specific concern for co-morbid conditions as outlined in Table 2. |

**Reference: TABLE 1: PASC Fatigue Assessment Recommendations** 

# **TABLE 2: Common PASC System Manifestations, Symptoms, Additional Testing/Studies and Referral Options**



|                | Further studies to consider in addition to basic laboratory evaluation   | Referral      |
|----------------|--|---------------|
| Cardiovascular | B-type natriuretic peptide (BNP), troponins, D-dimer, chest x-ray (CXR), electrocardiogram (EKG), echocardiogram (ECHO), exercise stress test/cardiopulmonary exercise test (EST/CPET), Holter monitor, cardiac magnetic resonance imaging | Cardiology    |
| Pulmonary      | D-dimer, pulmonary function tests (PFTs), CXR, computerized tomography (CT) chest (w/contrast if concerned for a pulmonary embolism)   | Pulmonology   |
| Endocrine      | Thyroid stimulating hormone (TSH)/Free T4 (thyroxine), cortisol levels, growth hormone, luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone (men), estradiol (women)  | Endocrinology |

### TABLE 2: Common PASC System Manifestations, Symptoms, Additional Testing/Studies and Referral Options



|                       | Further studies to consider in addition to basic laboratory evaluation   | Referral          |
|-----------------------|--|-------------------|
| Autoimmune            | Imaging of affected joints, antibody screen based on ongoing symptoms  | Rheumatology      |
| <b>Mood Disorders</b> | An anxiety and depression screen (for example, the Hospital Anxiety and Depression Scale (HADS), Beck Depression Inventory (BDI) fast screen; Patient Health Questionnaire (PHQ)-2/9, Geriatric Depression Scale (GDS) | Psychiatry        |
| Sleep Disorders       | Sleep apnea screen (for example, the STOP-BANG questionnaire or Epworth Sleepiness Scale (ESS)) overnight sleep study for oximetry and sleep apnea   | Sleep<br>Medicine |

## Relationship to ME/CFS



- Fatigue in individuals with PASC may appear similar to myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)
- Some individuals with PASC may later develop ME/CFS
- The majority of individuals with PASC do not meet ME/CFS diagnostic criteria, in the experience of the collaborative
- Diagnostic criteria for ME/CFS and additional information are available from CDC at <a href="https://www.cdc.gov/me-cfs">https://www.cdc.gov/me-cfs</a>
- The Collaborative's consensus guidance covers care of the general population of individuals with PASC, with consideration that individuals with PASC may have or develop ME/CFS

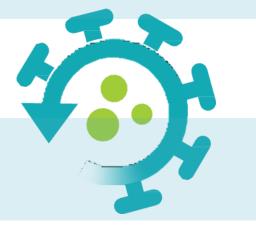
## **TABLE 4: PASC Fatigue Treatment Recommendations**



#### # Statement

Begin an individualized and structured, titrated return to activity program.

- <sup>2</sup> Discuss energy conservation strategies.
- Encourage a healthy dietary pattern and hydration.



Treat, in collaboration with appropriate specialists, underlying medical conditions, such as pain, insomnia/sleep disorders (including poor sleep hygiene), and mood issues which may be contributing to fatigue.

## **TABLE 4: PASC Fatigue Treatment Recommendations**



| Classification of PASC Fatigue | Definition   |
|--------------------------------|--|
| Mild                           | <ul> <li>Intact mobility</li> <li>Can perform activities of daily living and do light housework (often with difficulty)</li> <li>Able to continue working or going to school but may have stopped other, nonessential activities</li> <li>Often take time off, require modifications to their schedule</li> <li>Use weekends to recover from their work week.</li> </ul> |
| Moderate                       | <ul> <li>Decreased community mobility</li> <li>Limited in their performance of instrumental activities of daily living (particularly preparing meals, shopping, doing laundry, using transportation, and performing housework)</li> <li>Require frequent rest periods and naps and have generally stopped work or school.</li> </ul>                                     |
| Severe                         | <ul> <li>Individuals are mostly confined to the home</li> <li>May have difficulty with activities of daily living (eating, bathing, dressing, transferring, toileting, mobility) Leaving the home for these individuals is very limited and often leads to prolonged/severe after-effects.</li> </ul>  |

# PASC Fatigue Treatment Recommendation #1: aapm&r Mild fatigue

Begin an individualized and structured phased return to activity program

- Continue all household and community activities that have been tolerated with a slow return to higher intensity activities
- Exercise following the "rule of tens" increasing duration, intensity, and frequency of activity/exercise by 10% every 10 days
- Using the Rate of Perceived Exertion (RPE) scale, start at RPE 10—
   11/Light and progressing to 14-15/Hard on resumption of exercise.
- Go back to previous level if activity is not tolerated

# PASC Fatigue Treatment Recommendation #1: aapm&r Moderate fatigue

Begin an individualized and structured phased return to activity program

- Continuation of household and limited community activities that have been tolerated
- Patients should begin an activity or aerobic exercise program with exertion at sub-maximal levels, RPE 9–11/Very Light-Light
- Consider referral to a rehabilitation therapist with knowledge of post-COVID care to guide an individually titrated, symptom-guided program.
- Go back to previous level if activity is not tolerated

# PASC Fatigue Treatment Recommendation #1: aapm&r Severe fatigue

#### Begin an individualized and structured phased return to activity program

- Continue any household activities that have been tolerated without symptom exacerbation
- Begin a physical activity program, including upper and lower extremity stretching and light muscle strengthening before targeted aerobic activity
- Once tolerated, patients can begin an activity or aerobic exercise program at submaximal levels, RPE 7–9/Extremely to Very Light
- Consider referral to a physician with knowledge of post-COVID care (such as a physiatrist) to guide an individualized rehabilitation program
- Go back to previous level if activity is not tolerated

# PASC Fatigue Treatment Recommendation #2: aapm&r The Four Ps

#### **Energy conservation strategies**

- Pacing. Avoiding the push and crash cycle that is common in post-COVID recovery.
- **Prioritizing.** Encourages a patient to focus and decide on which activities need to get done and which activities can be postponed to avoid overexertion and crashing.
- Positioning. Modifying activities to make them easier to perform.
- **Planning.** Encourages the patient to plan the day or week to avoid overexertion and to recognize energy windows.

# PASC Fatigue Treatment Recommendation #2: aapm&r Returning to work accommodations:

#### **Energy conservation strategies**

- Working a limited number of hours
- Working from home
- Adjusting work activities
- Using durable medical equipment
- Additional breaks
- Adjusting the work environment
- Referral to vocational rehabilitation counselor can be helpful in structuring the return activities and communicating with employers

#### PASC Fatigue Treatment Recommendation #3: aap



Encourage patients to follow a healthy dietary pattern and stay hydrated throughout the day.

- No scientific data to support the "prescription" of one specific diet for the management of PASCrelated fatigue.
- Acute symptomatic COVID-19 is associated with a vigorous immune response and PASC theorized to be related to persistence of this immune dysregulation.
- Mast cell activation syndrome with histamine release suggested to play a role in PASC relatedfatigue.
- Some dietary recommendations have been made for individuals with ME/CFS, and similar dietary recommendations may be beneficial for PASC-related fatigue.
- Fatigue related to autonomic dysfunction in individuals with PASC, specifically postural orthostatic tachycardia syndrome (POTS), can be partially addressed with adequate water and salt intake.
- Fatigue due to muscle atrophy in the context of weight loss is reported in PASC and can be improved with appropriate caloric and protein intake.

## PASC Fatigue Treatment Recommendation #4: aapm&r

Treat, in collaboration with appropriate specialists, underlying medical conditions, such as pain, insomnia/sleep disorders (including poor sleep hygiene), and mood issues which may be contributing to fatigue.

## **TABLE 2: Common PASC System Manifestations, Symptoms, Additional Testing/Studies and Referral Options**

- Cardiovascular
- Pulmonary
- Endocrine
- Autoimmune
- Mood disorders
- Sleep disorders

### Pharmacologic therapy and supplements



There was no consensus on the use of supplements or medications.

- Some PASC-collaborative clinics do not use pharmacologic agents whereas others use agents when conservative management has been tried and comorbid conditions have been addressed.
- Patients often express interest in and desire for medications and herbal remedies/supplements. It is important to specifically ask patients about all products that they may be using in order to provide appropriate counseling.

## Other therapies



- The use of acupuncture has also been reported by collaborative patient representative members to improve fatigue.
- Although there has not been direct evidence to support its use in PASC-related fatigue, there is some preliminary low-quality evidence that supports its use in ME/CFS.

Health Equity Considerations and Examples in Post-Acute Sequelae







## **Example 1: Health Equity Considerations and Examples in Post- Acute Sequelae of SARS-CoV-2 Infection (PASC): FATIGUE**



| Category  | Comment   | What is Known   | Clinical Considerations   |
|---|---|---|---|
| Racial/Ethnic Minority Groups  Example: People who identify as Black (including African- American), American- Indian/Alaska Native, Pacific Islander, Asian- American, and Mixed Race, and/or | BIPOC (Black, Indigenous and People of Color) communities have been especially impacted by the global pandemic. worse outcomes after infection. | Social determinants of health, societal factors and structural racism have disproportionate effects on underinvested communities. | PASC-related fatigue is multifactorial, with its effects compounded for individuals already under the burden of racial and ethnic disparities and injustice.  Standardized treatment and management may decrease implicit bias. May require a multi-disciplinary approach to healthcare to address ongoing systemic |
| Latino/Hispanic (ethnicity)   |   |   | inequities.   |

## **Example 2: Health Equity Considerations and Examples in Post- Acute Sequelae of SARS-CoV-2 Infection (PASC): FATIGUE**



| Category   | Comment   | What is Known  | Clinical Considerations   |
|--|---|--|---|
| Biologic Sex  Characteristics  Example: Pregnant women | Physiologic and biologic sex differences should be considered for both the diagnosis and treatment of PASC-related fatigue. | Pregnant women frequently have pregnancy-related fatigue, and they may be at higher risk for more severe COVID-19 infections and symptoms, particularly women who have certain comorbidities and other characteristics (e.g., older age, diabetes, kidney disease, obesity). | Pregnant women who are status post COVID-19 infections may experience pregnancy-related fatigue in addition to PASC-related fatigue.  The risks and benefits of medications and other interventions should be assessed for both mother and fetus.  Exercise prescriptions may be impacted by symptoms such as excessive vomiting and weight loss in the 1st trimester and large girth, back pain, or pre-eclampsia in the 3rd |
|  |   |  | trimester.  |

## Health Equity Considerations and Examples in Post-Acute Sequelae of SARS-CoV-2 Infection (PASC): FATIGUE



## Example of Diversity, Equity, and Inclusion (DEI) Content Integrated into the Fatigue Consensus Guidance Statement

Symptoms of fatigue may be reported more commonly in female adults and in older age groups. (28) COVID-19 symptoms may be more severe in pregnant women (51) and pregnancy itself (and the post-partum period) is a well-known cause of fatigue due to a host of biologic and behavioral factors.

# Future Directions in Assessing and Treating PASC-Related Fatigue



- Individuals with PASC-related fatigue can experience a wide range of symptom severity, from bothersome to severe disability. Fatigue can lead to frustration and difficulty progressing with other treatment recommendations.
- The goal of this PASC Collaborative Consensus Guidance Statement is to create a coordinated and systematic approach to the evaluation and treatment of patients presenting with PASC.
- The recommendations represent a consensus of large national multidisciplinary collaborative of centers focused on the treatment of individuals with PASC.
- The recommendations are based on the most current available data, extrapolation from evidence in similar conditions, and the combined clinical experience of treating thousands of patients with PASC-related fatigue.
- The pathophysiology causing fatigue after COVID-19 still warrants ongoing research to better understand mechanisms and appropriate evaluation/treatment while acknowledging the cause of fatigue is likely multifactorial and may be specific to the individual.

Visit <u>www.aapmr.org/longcovid</u> to access the publication.



#### To Ask a Question

- Using the Zoom Webinar System
  - Click on the "Q&A" button
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- If you are a patient, please refer your question to your healthcare provider.
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When: A few hours after the live call ends

What: Video recording

 Where: On the COCA Call webpage https://emergency.cdc.gov/coca/calls/2021/callinfo 093021.asp

#### **Upcoming COCA Calls & Additional COVID-19 Resources**

- Thursday, October 7, 2021 (2:00 3:00 PM ET): 2021–2022 Recommendations for Influenza Prevention and Treatment in Children: An Update for Pediatric Practitioners (Free CE) (https://emergency.cdc.gov/coca/calls/2021/callinfo 100721.asp)
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As-needed messages that provide specific, immediate action clinicians should take. Contains comprehensive CDC guidance so clinicians can easily follow recommended actions.

#### **COCA Products & Services**







Monthly newsletter providing updates on emergency preparedness and response topics, emerging public health threat literature, resources for health professionals, and additional information important during public health emergencies and disasters.

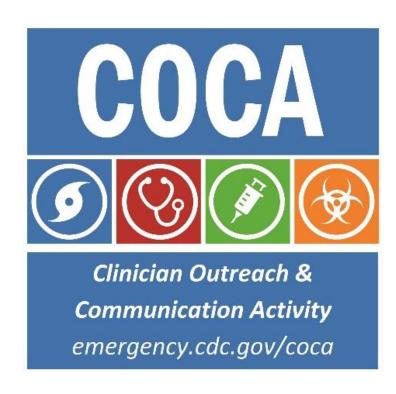
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